

### **REMARKS**

Applicants thank the Examiner for the courtesy extended during a March 16, 2011 telephone conference to discuss the pending Office Action. Applicants appreciate the opportunity to discuss the issues remaining in the case.

Claims 21-24, 28-38, 40-42, 46, 48-54, 56, 57, 63-66, and 68-75 are pending in this application. Claims 21, 22, 38, 63, 65, and 68-73 have been amended. Claims 1-20, 25-27, 39, 43-45, 47, 55, 58-62, and 67 are cancelled. Independent claims 21, 22, and 38 are amended to correct typographical errors. Dependent claims are amended to either correct typographical errors or to correct their dependencies from an independent claim. Dependent claims 68, 70, and 72 were also amended to delete reference to a trademark. No new matter is added.

### **Rejection under 35 U.S.C. § 112, Second Paragraph**

The Examiner rejected Claims 68, 70, and 72 as indefinite for reciting a trademark. Applicants have amended the claims to delete reference to trademarks. Accordingly, this rejection can be withdrawn.

### **Rejections under 35 U.S.C. § 103**

Claims 21-24, 28-38, 40-42, 46, 48-54, 56, 57, 63-66, and 68-75 remain rejected as unpatentable over Muller and Andersson. The rejection is traversed to the extent it is applied to the claims as amended.

### **A Claimed Composition is Nonobvious when it Possesses Different Properties**

A claimed composition is nonobvious when it possesses characteristics different from the one disclosed in the prior art. See § 2112.01(I) of the M.P.E.P. (stating that that a prima facie case of obviousness can be rebutted by showing that the prior art products do not possess the characteristics of the claimed product)

In the Office Action of December 22, 2010, the Examiner maintains that the claims are unpatentable over Muller in view of Andersson, asserting that an autoclaved composition comprising trehalose with water insoluble drug and phospholipid would have been obvious based on the two references. In the Office Action and during the interview, Examiner reiterated that the presence of trehalose in combination with a water insoluble drug and a phospholipid reads on the claimed invention, regardless of the function of each component.

Applicants respectfully disagree. In the response filed on October 19, 2010, Applicants argued that an ordinary artisan would not rely on Muller because the reference teaches different methods to derive compositions much different from the claimed invention and with different properties. In preparing the suspensions of microparticles, Muller experimented with several surfactants and stabilizers known in the art (for *e.g.*, Tween 80, polyvinyl alcohol, Polyacrylates, poloxamers, and poloxamines), in order to enhance the viscosity of the carrier composition (*see, e.g.*, Muller, claim 21). Furthermore, in an attempt to stabilize the nanosuspensions, Muller experimented with varying the concentrations of Tween 80, as a surfactant when the compositions were autoclaved, or added a viscosity enhancing agent when the composition was not autoclaved but pumped through a homogenizer. *Compare* Muller, Examples 10-12, with Example 13; col. 8, lines 25-33.

Thus, Muller teaches at least two distinct methods: the first involving autoclaving a surfactant containing composition and the second involving pumping a composition lacking surfactant through a homogenizer but without autoclaving. Muller discloses that particle size increases after autoclaving. *See* Muller, Figure 14. In addition, homogenization of the particles allows increase in solubility by an increase in surface tension. *See id.* at col. 6, lines 28-32.

Further, both methods described in Muller included viscosity increasing agents. *See id.* at claim 21, *and* col. 8, lines 27-33. While viscosity of particles prepared by autoclaving was increased by including Tween 80 (a surfactant; *see id.* at col. 7, lines 25-27; *see also* claim 21), viscosity of particles prepared by homogenization was increased with sodium

carboxymethylcellulose to avoid the problem of increased sedimentation during pumping through the homogenizer (*see id.* at col. 17, Example 13, and col. 8, lines 27-33).

Unlike in Muller, no surfactant or any viscosity increasing excipients were added in the composition of the current invention because any increase in viscosity of microparticle composition was undesirable. While in Muller, poloxamer or polyvinyl alcohol was added to increase viscosity during autoclaving (*see, e.g.*, Muller, claim 21), these excipients were avoided in the current invention because they have a natural tendency to coagulate at high temperature. *See* Specification of Current Application, page 4, ¶ 1. Indeed, Applicants found that the addition of surfactant resulted in large increase in particles sizes and significant increase in viscosity after autoclaving; both undesirable properties of the composition. *See id.* at 8, ¶ 5 - 9, ¶ 1. Thus, the composition lacking a surfactant obtained by the method in the current application ensures that the mean diameter of the particles in the suspension does not increase more than between 1.04-1.18 after steam sterilization, and viscosity does not increase significantly. *See id.* at 5, ¶¶ 4-5; 9, ¶ 1.

The claimed invention is therefore nonobvious because Muller teaches at least two distinct methods to derive different compositions, which are distinct in characteristics from the claimed composition.

The current invention is further distinguishable from Muller because, unlike in example 13 in Muller, which requires a viscosity enhancing agent to reduce sedimentation during pumping through the homogenizer, in the current invention sedimentation of the particles was not a problem after steam sterilization, as the "formulation could not be sedimented by centrifuging for approximately 20 min at 3000-rpm." (*See* Specification, page 11, Example 6.) Because sedimentation is not a problem in the composition prepared by the method of the current invention, the composition requires no viscosity increasing excipients to prevent sedimentation (*see* Muller at col. 8, lines 30-33). Thus, Muller employs distinct methods to achieve distinct products with distinct characteristics.

Applicants, therefore, believe that the Examiner's finding of *prima facie* obviousness is improper and request reconsideration and withdrawal of the rejections.

## II. A Prior Art Reference Must be Considered in Its Entirety

In considering the disclosure in the prior art, § 2141.02(a)(VI) of the M.P.E.P. requires that the Examiner considers the prior art as a whole, rather than specific teachings in the art. *Id.* (“A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.”) (Emphasis in original).

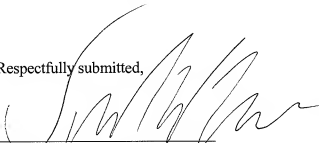
The Examiner has relied on Andersson for teaching only “autoclaving” under “nitrogen” conditions. As discussed above, the Examiner avoided taking into account Muller at its entirety, but has combined at least two distinct excipients and processes to conclude that the claimed composition is obvious over the reference. In combining Muller with Andersson, the Examiner again avoided considering the entire disclosure in Andersson, thus finding the claimed invention *prima facie* obvious over the combination of the references.

The artisan considering the teachings in Andersson as a whole would interpret it to require a composition including glycerol (*see* Andersson, col. 6-7, Examples 1-11). Unlike in Andersson, the current invention relies on the finding that glycerol destabilizes particles after autoclaving. Thus, based on the teachings in Andersson, in its entirety, when combined with the teachings in Muller requiring surfactants or viscosity increasing agents, one of the ordinary skills in the art will derive a composition distinct from that in the current invention. In fact, the composition so derived would be undesirable because glycerol would destabilize, and surfactants or other viscosity increasing agents will lead to significant increase in size and viscosity of the microparticles after steam sterilization. Applicants, therefore, believe that the Examiner’s finding of *prima facie* obviousness is improper and request reconsideration and withdrawal of the rejections.

**CONCLUSION**

Applicants submit that the application is in condition for allowance and request an action for the same. A petition for an extension of time accompanies this response. Please charge any additional fees due, or credit any overpayment of same, to Deposit Account 50-0311, Attorney Reference No.: 28069-503001US.

Respectfully submitted,



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